REMARKS

Claims 1, 4, 8 and 9 are pending herein. Claim 1 has been amended to include the subject matter of claims 2 and 3. Claims 2 and 3 have been cancelled. Claims 5-7 were withdrawn via the Reply to Restriction Requirement filed by Applicants on 6/5/2008. Based on the above amendments to the Claims and the following remarks, Applicants believe the instant application is in condition for allowance.

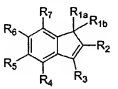
1) **Rejection under 35 U.S.C. §112 – Claims 1 to 3, 8 and 9**

The Examiner rejected claims 1-3, 8 and 9 by stating that the scope of formula (I) recited is overly broad in view of the subject specification. Applicants have amended Claim 1 to include the subject matter of Claims 2 and 3 and believe that the scope of formula (I) as recited currently, in conjunction with Table 1 of the Specification, wherein specific compounds are listed as being within the scope of formula (I), should serve to overcome the rejection under 35 USC 112, first paragraph. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn and the application be forwarded to issue.

2) **Rejection under 35 U.S.C. §102 over WO 93/08799**

The Examiner rejected claims 1, 2, 8 and 9 under 35 U.S.C. §102(b) as being anticipated by WO 93/08799 ("Cousins"). Applicants respectfully traverse this ground of rejection as follows.

The subject matter of the present invention, as recited in amended Claim 1, is for and indene derivative of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein,

R_{1a} is OH or H;

R_{1b} is C_{1-6} alkyl, C_{3-6} cycloalkyl, benzyl or phenyl, the phenyl being optionally substituted with one or more methoxy groups, when R_{1a} is OH; when R_{1a} is H, R_{1b} is OR^i, NR^bR^c, $NHCOR^i$ or 
R_2 is CN, CO_2R^a or $CONR^j$;
R_3 is phenyl;
R_4, R_5 and R_7 are H; and
R_6 is $O(CH_2)_mR^g$ or CH_2R^h;
in which
R^a is H or C_{1-6} alkyl;
R^b, R^c, R^e and R^f are each independently H, C_{1-6} alkyl, C_{3-6} cycloalkyl or benzyl;
R^d is O;
R^g is H, pyridine,  r phenyl;
R^h is
R^i is C_{1-6} alkyl;
R^j is C_{3-6} cycloalkyl; and
m is an integer in the range of 1 to 3.

Cousins fails to disclose an indene derivative which is substituted by R^6, i.e., OCH_3, as in formula (I) of the present invention. Accordingly, Claim 1 as, amended, is not anticipated by Cousins, and, therefore, this ground of rejection should be withdrawn.

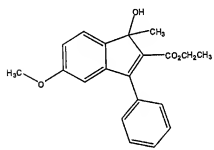
Furthermore, Claim 1 relates to an indene derivative selectively modulating the activities of peroxisome proliferator activated receptors (PPARs), which is useful for the treatment and prevention of disorders modulated by PPARs. Therefore, the subject invention is different from Cousins in terms of the pharmacological mechanism. Moreover, the indene derivative of Claim 1 does not cause any side effects, such as weight gain, cardiac hypertrophy, edema and liver damage, which a conventional PPARγ full antagonist has. Such remarkable effects of the subject invention cannot be easily expected from Cousins merely referring to a pharmaceutical composition containing indene derivatives as an endothelin receptor antagonist. Namely, the indene derivative of the subject invention is not specifically disclosed in Cousins and the subject invention has qualitatively different working effects compared with Cousins, and, thus, the subject invention is novel and inventive over Cousins.

3) **Rejection under 35 U.S.C. §102(b) and 103(a) over Rayabaparu**

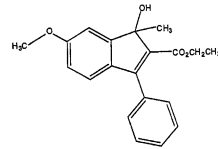
The Examiner rejected claims 1 to 3 under 35 USC 102(b) as being anticipated by Rayabarapu et al. (J. Org. Chem., vol. 68, p6726-6731, 2003) ("Rayabarapu"). In addition, the Examiner rejected Claims 1-4 as being obvious over Rayabarapu. Applicant respectfully traverse both of these grounds of rejection as follows.

Rayabarapu discloses an indenol derivative whose 5-position is substituted by OCH_3 and 6-position is unsubstituted, unlike formula(I) of the present invention, as recited in amended Claim 1. which requires that the 6 position be substituted instead of the 5 position, as shown below :

Rayabarapu



the subject invention



Accordingly, amended Claim 1 is not anticipated by Rayabarapu, and, therefore, this ground of rejection should be withdrawn.

With regard to the obviousness rejection under 103(a) over Rayabarapu, Rayabaraopu disclose regioselective synthesis of indenols. The Examiner states on Pages 9-10 of the Office Action that "the difference between the instant compound and that of the prior art is that the instant compound has methyl group instead of butyl in the position 1 and is ethyl ester rather than methyl ester." A visual comparison of the two compounds is shown above, and it is clear that, in fact, as stated, supra, Rayabarapu discloses an indenol derivative whose 5-position is substituted by OCH_3 and 6-position is unsubstituted, unlike formula(I) of the present invention. Rayabarapu et al are quite clear that the compounds disclosed in their article are "completely regioselective" Page 6727, Column 2, 2nd paragraph, last line. Accordingly, that prior art teaches away from

compounds that vary from those listed in its Tables. In addition, , Rayabarapu does not disclose the pharmaceutical use of an indene derivative. Rayabarapu merely disclose a regioselective synthesis of indenols via nickel catalyzed carbocyclization. There is no teaching suggestion or motivation that would lead one of ordinary skill in the art to the present invention based on the disclosure of Rayabarapu.

CONCLUSION

Based on the foregoing amendments to the claims and remarks, Applicant submits that the instant application is in condition for allowance and should be forwarded to issue.

Respectfully submitted,

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Dated: October 3, 2008

CUSTOMER NO.: 79681

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CERTIFICATE OF TRANSMISSION

I hereby certify that this Amendment is being submitted to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via EFS-Web on October 3, 2008.

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Audrey de Souza